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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,676	02/28/2002	Iris Ziegler	148/50932	2539

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,676	ZIEGLER ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, foreign priority paper and remarks filed 03/22/04.

Examiner acknowledges receipt of translation of the foreign priority paper DE 199 40 944.7. The prior art previously cited under 35 USC 102(b) will now be cited under 35 USC 102(e) since a translation of the priority document is provided.

1. Applicants' arguments with respect to claims 17 and 38 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 102

2. Claim 17 is rejected under 35 U.S.C. 102(e) as being anticipated by Mauskop (US 5,914,129).

Mauskop discloses magnesium containing analgesic oral composition for the treatment/alleviation of pain, and specifically migraine headache pain (abstract). Solid formulations of the composition are capsules, catchets or tablets and powder or granules; liquid formulations are solution or suspension in aqueous liquid or non-aqueous liquid and oil-in-water or water-in-oil emulsions; and solid formulation of tablet and capsules are preferred with tablet being the most preferred (column 6, lines 12-21). In a particular embodiment of Mauskop, the magnesium containing analgesic composition includes at least two different non-opioid analgesic agents, at least two different opioid analgesic agents or at least one non-opioid analgesic agent and at least one opioid analgesic agent and it is believed that a combination of non-opioid

analgesic agents or opioid analgesic agents or a combination of non-opioid and opioid analgesic agents act synergistically to relieve pain (column 3, lines 47-54). In the case where the pharmaceutical composition comprises a combination of a non-opioid analgesic agent and an opioid analgesic agent (claim 6); the non-opioid analgesic agent of ibuprofen, naproxen and diclophenac (diclofenac sodium) are included in the list of non-opioid analgesic agents provided (claims 1-4, 6 and 15) and the opioid analgesic agents of tramadol is included in the list of opioid analgesic agents provided (claims 1, 4, 5, 6 and 17); specifically pharmaceutically acceptable salts such as the hydrochloride salt is employable (column 3, lines 10-14). Mauskop, in column 6, lines 18-31, discloses how the tablet is formulated. Mauskop discloses a combination of opioid analgesic and non-opioid analgesic to synergistically act to relieve pain (column 3, lines 47-54) and tramadol hydrochloride and diclofenac sodium are included in the list provided (column 3, lines 1, 8 and 12). The property of a composition is not separable from the composition and how a composition is made is not critical. Instant claim 17 reads on a composition that contains diclofenac sodium and tramadol hydrochloride. Mauskop meets the limitations of the claim.

Applicants argue that:

a) The compound of claim 17 is prepared per paragraph [0011]-[0013]. Applicants further state that "paragraphs 17, 18 and 21 also relate to in situ formation of certain embodiments of the compound," and that the in situ formation of the compound influences the solubility of the compound in water; that the in situ formed compound "causes the oral pharmaceutical form of administration to be at least partially sustained release." Applicants further state that in some embodiments, tramadol release is at least partially retarded without the

use of sustained release matrix and/or sustained release coating and that part of diclofenac and part of tramadol are released at the same time, which is not the case where tramadol hydrochloride and diclofenac sodium are separate compounds within a composition.

b) Applicants argue that Mauskop does not teach or suggest a compound of tramadol hydrochloride and diclofenac sodium. Applicants argue that Mauskop does not teach or suggest the in situ formation of a compound of tramadol hydrochloride and diclofenac sodium. That Mauskop does not teach or suggest a compound of tramadol hydrochloride and diclofenac sodium that has a solubility of $\leq$ 100 mg/ml.

3. Applicants' arguments filed 03/22/04 have been fully considered but they are not persuasive.

4. Regarding a), it is noted that instant claim 17 reads on a composition and each of the tramadol hydrochloride and the diclofenac sodium are compounds in themselves. While applicants refer to paragraphs [0011]-[0013], 18, 18 and 21, it is respectfully noted that limitations from the specification cannot be read into the claims, (see *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993)). Secondly, how the composition or compound is formed is not critical to patentability of the compound or composition. The release of tramadol or diclofenac is a property of the composition or the compound. It is also noted that instant claim 17 does not recite specific amounts of the respective drugs in the composition that distinguishes the instant claim 17 from the disclosed composition of the prior art. Regarding the issue that in some embodiments the release of tramadol is partially retarded without the use of sustained release matrix or coating, it is noted that the embodiment claimed is a compound of tramadol hydrochloride and diclofenac sodium. Also, claim 17 reads on a composition that

comprises tramadol hydrochloride and diclofenac sodium. If a chemical compound form between the individual compounds of diclofenac sodium and tramadol hydrochloride, the compound would appear to have different properties from the individual compounds. Secondly, there is no description of the supposed compound formed between the two compounds. What is the name of the resultant compound formed between the two individual compounds? Do the individual compounds retain the individual properties of characteristics within the supposed compound? How would it be that each compound is released from the supposed compound with out alteration of the compound? At least, the claim 17 does not read on a prodrug, where hydrolysis of the linkage releases the active drug. From the point of view of the examiner, the compound reads on a composition that comprises tramadol hydrochloride and diclofenac sodium. No sustained release matrix is claimed that would distinguish the instant composition/compound from the disclosed composition of the prior art.

Regarding b), the solubility of the tramadol hydrochloride and diclofenac sodium composition is a property of the composition. Instant claim 17 reads on a composition or compound comprising two component drugs. Applicants' insistence of a compound of tramadol hydrochloride and diclofenac sodium is not apparent because for tramadol hydrochloride and diclofenac sodium to form a compound, the chemical reaction would be such that a new compound be formed that would have distinct characteristics and properties from the individual drugs. What is the name and structure of the compound formed from the tramadol and diclofenac and would each drug be released from the compound without alteration of the properties and integrity of the tramadol and the diclofenac?

Claim Rejections - 35 USC § 103

5. Claim 38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mauskop (US 5,914,129).

Mauskop discloses a composition comprising tramadol and diclofenac and a method of preparing the composition. Mauskop in column 6, lines 11-31 discloses forming tablets by conventional method of compression and molding and specifically discloses that molded tablets and be optionally moistened with an inert liquid diluent. The instant method comprises a mixing of tramadol hydrochloride and diclofenac sodium, which the prior art discloses. The instant method comprises a moistening step which the prior art discloses. Repeating the mixing and moistening steps is an obvious variant of the method at the disposal of the person of ordinary skill in the art or to the skilled artisan to whereby the steps are repeated as necessary for the production of the desired tablet. Mauskop does not specifically disclose formulating the mixture under energy input. However, compressing or granulating the mixture requires some form of energy input (see the eighteenth edition of Remington's Pharmaceutical Sciences, 1990, pages 1641-1647 as a teaching reference in the compression and granulation of pharmaceutical preparations). However, a method of making compositions are disclosed and taught in the eighteenth edition of Remington's Pharmaceutical Sciences. Remington specifically teaches wet-granulation method, fluid-bed granulation method, dry-granulation method, direct compression and related granulation processes (pages 1641-1647). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate the preparation of Mauskop by mixing and moistening the mixture as disclosed by Mauskop.

One having ordinary skill in the art would have been motivated to apply the necessary energy to the mixture with the expectation of producing tablets.

Double Patenting

6. Claim 17 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 11 of copending Application No. 10/016,130. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 17 is directed a composition comprising tramadol and diclofenac; claim 1 of the copending application teaches a composition that comprises tramadol and diclofenac. The solubility and the release rate recited in instant claim 17 are properties and the property of a composition is not separable from the composition. The instant claim 17 does not exclude separate subunits. Applicants argue that the co-pending application teaches separate subunits and the in the instant claim, diclofenac and tramadol are formulated together. This argument is not persuasive because the instant claim does not exclude separate subunits and it appears that the separate subunits are formulated as one unit for administration.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 242-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
Tech. Center 1600